Derivaten van alfa-aminosulfonen

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SUMMARY

The aim of the research presented in this thesis is the synthesis of *N*-substituted α-aminosulfones and a study of some reactions of these compounds.
In chapter 2 an efficient one-step synthesis of *N*-substituted α-aminosulfones is described, *i.e.* a Mannich-type condensation of sulfinic acids with aldehydes and carbamates, (di)thiocarbamates, carboxamides, lactams and sulfonamides respectively.

$$RSO_2H + R'CHO + R''NHY \xrightarrow[H_2O]{HCO_2H} RSO_2CHR'NR''Y + H_2O$$

R = alkyl, aryl.

R', R'' = H, alkyl, aryl
Y = CO_2R''', $C(S)OR'''$, $C(O)SR'''$, CS_2R''', $C(O)R'''$, SO_2R'''.

The scope of the condensation of sulfinic acids with an aldehyde (aliphatic or aromatic) and the nitrogen bases employed has been investigated by variation of R, R', R'' and Y. In several cases the condensation products were rather unstable compounds. A possible mechanism for the condensation reaction involves addition of the nitrogen base to the aldehyde as the first step. Subsequent dehydratation gives a resonance-stabilized carbonium ion that upon reaction with a sulfinate anion affords the isolated products. The PMR spectra of most of the products derived from *N*-substituted carbamates and (di)thiocarbamates showed interesting features due to hindered internal rotation and conformational preferences.

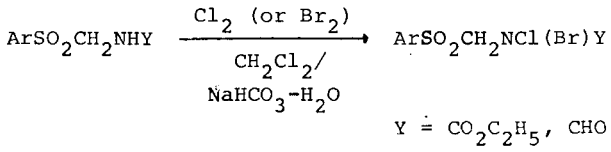
Those derivatives of α-aminosulfones, which possess an activated hydrogen at the nitrogen atom, react smoothly with certain nucleophiles in the presence of a sufficiently strong base (chapter 3). Under these conditions sulfinic acid is eliminated to give an aldimine R'CH=NY, which reacts easily with nucleophilic reagents ZH. This is examplified by the reaction with secondary aliphatic amines, thiols and methanol.

$$RSO_2CHR'NHY \xrightarrow{base} \left[R'CH{=}NY\right] \xrightarrow{ZH} ZCHR'NHY$$

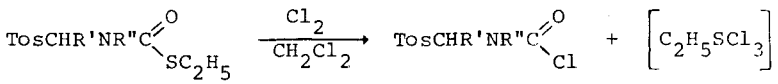
The *N*-sulfonylmethylcarbamates, -thiocarbamates and -carboxamides with R' = H may also add to the intermediate aldimine. Reduction of the C = N bond of the aldimines could be accomplished with $NaBH_4$. Attempts to obtain the Diels-Alder addition product of the aldimines (prepared *in situ*) with representative dienes were unsuccesful.

The final chapter of this thesis (chapter 4) deals with the reactions of *N*-(1-tosylalkyl)carbamates, -carboxamides and -(di)thiocarbamates with chlorine and bromine.

The *N*-arylsulfonylmethylcarbamates and -carboxamides were easily converted into the corresponding *N*-chloro(or bromo) derivatives.

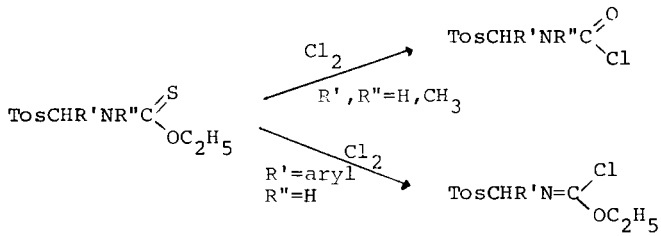


However, *N*-(1-tosylalkyl)monothio- and -dithiocarbamates reacted in a completely different way, affording products formed by chlorine or bromine attack on the sulfur atom(s) of the thiocarbamate moiety. Upon treatment with chlorine under anhydrous conditions the *S*-ethyl *N*-(1-tosylalkyl)thiocarbamates were transformed into *N*-(1-tosylalkyl)carbamoylchlorides.

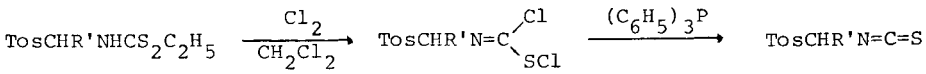


In the presence of a weak base, which is unable to bring about elimination of *p*-toluenesulfinic acid, the *S*-alkyl thiocarbamates with R'' = H react with chlorine to yield the corresponding 1-tosylalkylisocyanates.

The *O*-alkyl *N*-(1-tosylalkyl)thiocarbamates with R' and R'' = H or CH_3 were also transformed into *N*-(1-tosylalkyl)carbamoylchlorides by action of chlorine, in contrast to the thiocarbamates with R' = aryl and R'' = H, which gave *N*-(α-tosylbenzyl)chloro ethoxyformimides.



The *N*-(1-tosylalkyl)dithiocarbamates react with chlorine at room temperature yielding *S*-chloro-*N*-(1-tosylalkyl)isothiocarbamoylchlorides. These compounds were easily transformed by triphenylphosphine into 1-tosylalkylisothiocyanates.



When the reactions of the dithiocarbamates with chlorine were carried out at higher temperatures, *N*-(1-tosylalkyl)dichloroformimides (TosCHR'N = CCl_2) could be isolated. Possible mechanisms for the reactions with halogens are proposed.